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## Now dear, I have a headache! Immediate improvement of cluster headaches after sexual activity

The precise pathogenesis of cluster headaches is unknown, but a hypothalamic generator has been postulated as the cause of the disorder.<sup>1</sup> In two patients with typical cluster headaches, sexual activity alleviated the episodes. This association may shed some light on the pathogenesis and treatment of this incapacitating disorder.

**Patient 1:** A 61-year-old, previously healthy man presented with excruciating, left-sided orbital headaches appearing in bouts that lasted for 10 weeks. The pain occurred nightly at around 22:00 h, and was associated with ipsilateral ptosis, lacrimation and rhinorrhoea. Neurological examination and brain imaging were normal and he was diagnosed with cluster headaches, according to International Headache Society (IHS) criteria.<sup>2</sup> The headaches always lasted for 90–150 min, except for instances when the patient had sexual intercourse, which at the point of orgasm resulted in instant dramatic improvement in the pain, with complete relief always being achieved within several minutes and no recurrence until the next evening. Orgasm occurred on six occasions between 5–30 min after the onset of the episode and termination of the episode followed in all instances. Prophylactic treatment with verapamil was initiated and he was advised to try oxygen inhalation. Adherence to this regimen abolished the current cluster of headache episodes.

**Patient 2:** A 47-year-old previously healthy man had episodes of headache appearing in clusters since his teens. Episodes consisted of unilateral orbital pain with lacrimation and rhinorrhoea that lasted for 30–60 min, with a frequency of 1–3 episodes daily for several weeks. His headaches fitted IHS criteria for cluster headache.<sup>2</sup> For two decades, he was treated with triptans and prophylactic indomethacin, and rarely had headaches. Cessation of the treatment was followed by relapse. More than a decade after discontinuing treatment, he consulted a neurologist and

reported that over the years he had learnt that sexual intercourse and masturbation were linked with instant relief from the headache at the point of orgasm. Neurological examination and brain imaging were normal. Prophylactic treatment with indomethacin was reinstituted, with no episodes reported over the subsequent 2 years of follow-up.

## Discussion

The link between sexual activity and cluster headaches has been discussed before. Patients with cluster headaches (but not healthy controls) respond to testosterone administration by increasing their sexual behaviour, which may suggest a derangement of central nervous system processes associated with libido.<sup>3</sup> The case of a patient who had cluster headaches which disappeared during the period of involvement in a sexual relationship but subsequently relapsed after the termination of the relationship, has been described.<sup>4</sup> Although cluster headaches have been reported to be triggered by intercourse,<sup>4</sup> in our patients the headache was well established before the initiation of sexual activity.

Our observation is novel in that it documents the termination of individual cluster headache episodes by orgasm and could relate to one or more of the processes underlying the pathophysiology of cluster headaches. According to the “gate theory”, sexual activity may activate inhibitory pain-modulating circuits.<sup>5</sup> This phenomenon occurs in many situations in which there is a survival value in not “giving-in” to pain, and may also be responsible for the placebo effect. Related to this process is the possibility that reduction in headache could be related to endorphin excretion, which occurs after sexual arousal and orgasm.<sup>6</sup>

While these pain-reducing processes could equally apply to any nociceptive experience, more specific neuroanatomical relationships between sexual activity and cluster headaches exist. The episodic nature of cluster headaches suggests the involvement of a central impulse generator or oscillator, and a biological clock within the hypothalamus has been implicated.<sup>1</sup> Positron emission tomography scanning showed an intense activation of the posterior hypothalamus during an episode, and refractory patients respond to hypothalamic deep brain stimulation.<sup>7</sup> Intriguingly, orgasm is accompanied by intense hypothalamic activation.<sup>8</sup> Thus, it can be postulated that orgasm terminates cluster headaches by modulating hypothalamic circuits in a manner similar to that which occurs in deep brain stimulation.

Patient 2, although satisfying IHS criteria for cluster headaches, is notable for his response to indomethacin. Although cluster headaches have been reported to respond to indomethacin,<sup>9</sup> this feature usually suggests paroxysmal hemicrania<sup>2</sup> and raises the possibility that this phenomenon may be relevant to the trigeminal autonomic cephalgias (TAC) as a group, all of which are associated with the posterior hypothalamus.<sup>9</sup>

The sympathetic nervous system is believed to be associated with TAC in a passive manner<sup>1</sup>; however, in some cases, there is evidence of sympathetic dysfunction before the onset of TAC,<sup>10</sup> suggesting that sympathetic underactivity may underlie TAC pathogenesis. If TAC pain is dependent on low sympathetic tone, theoretically the episode

could be reversed by the increase in sympathetic activity accompanying sexual activity and, specifically, orgasm.

Patients with TAC may be reluctant or unable to engage in intercourse during an episode or disinclined to volunteer such information. Given that other sufferers may potentially benefit from this phenomenon, and as it has relevance to the pathogenesis of TAC, this observation should be verified in a large cohort of patients.

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## Novel Olig1-coding variants and susceptibility to multiple sclerosis

Olig1 is a basic helix–loop–helix (bHLH) transcription factor expressed in cells of the oligodendrocyte lineage in the nervous system. Its role during normal development has not yet been fully resolved, but it is known that in adult life the protein is crucial in the process of remyelination after injury.<sup>1–3</sup> Olig1 translocates from the cytoplasm to the nucleus in early remyelinating lesions in rodent models of demyelinating disease as well as in oligodendrocyte precursor cells at the edge of multiple sclerosis lesions.<sup>1</sup> Olig1 specifically regulates the expression of the